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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,527	BOUGUELERET, LYDIE	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *82-127* is/are pending in the application.

4a) Of the above claim(s) *124-127* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *82-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

This application is a 371 of PCT/IB99/01353.

The amendment filed on November 29, 2004, canceling claims 43-76 and 78-81 and adding claims 82-127, has been entered.

Claims 82-127 are pending. Claims 124-127 are withdrawn. Claims 82-123 are under consideration.

Election/Restrictions

Newly submitted claims 124-127 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 124-127 are drawn to a method of making a hGGPPS by transforming a host cell with a polynucleotide encoding said protein. The elected claims are drawn to a polypeptide. These claims would have been placed in Group I, drawn to polynucleotides encoding hGGPPS and methods of making hGGPPS, see the Office Action mailed on September 25, 2002.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 124-127 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Arguments

Applicant's amendment and arguments filed on November 29, 2004, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 82-123 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Claims 82-123 are drawn to polypeptides consisting of 6-55 or 100 amino acids of SEQ ID NO:4 having GGPPS activity or wherein the polypeptides bind to hGGPPS or its fragments. It is this part of the claims that Examiner takes the position that said fragments lack utility. Even though the claims recite that the polypeptides having GGPPS activity, the claimed polypeptides are not supported by either a specific and substantial asserted utility. The specification fails to provide objective evidence of any activity for the polypeptides consisting of short fragments of SEQ ID NO:4 except that it binds to hGGPPS or its fragments. Therefore, no specific, substantial and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material is indicated. Merely stating that a polypeptide binds to another peptide does not set forth a specific substantial or credible utility. Therefore, there is no specific, substantial, or credible utility that is well known,

apparent, or implied by the relationship of the instant fragments to the polypeptides having GGPPS activity.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 82-123 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide of SEQ ID NO:4 having GGPPS activity, does not reasonably provide enablement for polypeptides consisting of fragments of SEQ ID NO:4 or its fusion polypeptides, wherein said polypeptides have no specific function or any function, except for binding to antibodies that bind to hGGPPS, fragment of hGGPPS or a contiguous span of at least 6 amino acid of SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.

1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 82-123 are drawn to a polypeptide consisting of fragments of SEQ ID NO:4, wherein said polypeptide binds to antibodies that bind to a) hGGPPS, b) fragment of hGGPPS, or c) a contiguous span of at least 6 amino acids of SEQ ID NO:4. Binding between a fragment of SEQ ID NO:4 and antibodies that bind to a)hGGPPS, including any variants, mutants or recombinants, b) fragment of hGGPPS, including any variants, mutants or recombinants, or c) a contiguous span of at least 6 amino acids of SEQ ID NO:4, does not impart any function to said fragments of SEQ ID NO:4. Therefore, many functionally unrelated polypeptides are encompassed within the scope of these clams, including partial amino acid sequences. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The specification does teach how to make polypeptides consisting of fragments of SEQ ID NO:4, wherein the polypeptides have GGPPS activity, but not polypeptides having any function or no activity. The function of a polypeptide cannot be predicted from its structure and the specification does not teach how to use polypeptides having any function or having no activity. The quantity of experimentation to determine activity and use of the polypeptide is extremely large since there can be significant variability in the activity of the polypeptides in the claims. It would require significant study to identify

the actual function of the polypeptides and identifying a use for the polypeptide would be an inventive, unpredictable and difficult undertaking. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The art is extremely unpredictable with regard to protein function in the absence of realizable information regarding its activity. Even very similar proteins may have every different functions. In the current case, where no specific information is known regarding the function, it is entirely unpredictable what function and activity will be found for the protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the fragments and their fusion proteins.

It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the making and use of polypeptides consisting of fragments of SEQ ID NO:4, wherein the polypeptides have GGPPS activity, but provides no guidance with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polynucleotides encompassed by the claims.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions

within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides consisting of fragments of SEQ ID NO:4, wherein the polypeptides have any function. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination and use of polypeptides consisting of fragments of SEQ ID NO:4 having any function is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 82-123 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 82-123 are drawn to a polypeptide consisting of fragments of SEQ ID NO:4 and fragments of SEQ ID NO:4 fused to heterologous polypeptides, and

fragments of SEQ ID NO:4 fused to heterologous polypeptides, wherein said polypeptide binds to antibodies that bind to a) hGGPPS, b) fragment of hGGPPS, or c) a contiguous span of at least 6 amino acids of SEQ ID NO:4. Binding between a fragment of SEQ ID NO:4 and antibodies that bind to a)hGGPPS, including any variants, mutants or recombinants, b) fragment of hGGPPS, including any variants, mutants or recombinants, or c) a contiguous span of at least 6 amino acids of SEQ ID NO:4, does not impart any specific function to said fragments of SEQ ID NO:4. Therefore, many functionally unrelated polypeptides are encompassed within the scope of these clams, including partial amino acid sequences. The genus of these polypeptides comprise a large variable genus with the potentiality of encompassing many different proteins having different activity or no activity. The specification only describes polypeptides consisting of fragments SEQ ID NO:4 having GGPPS activity. The specification fails to describe additional representative species of the polypeptides by any identifying characteristics or properties of the polypeptides other than the structural characteristics recited in the claims, for which no predictability of function is apparent, and that the polypeptides bind to antibodies that bind to any or all fragments of human GGPPS, including recombinants, variants and mutants. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention

in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 82-123.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 96 and 109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 96 and 109 recite the phrase "contiguous span consists of amino acid positions 200 through 300 of SEQ ID NO:4". The polypeptide encompassed in the claims consists of more than 100 contiguous amino acids. However, claims 96 and 109 ultimately depend from claim 82, which limits the length of the polypeptides to a maximum of 100 contiguous amino acids selected from SEQ ID NO:24 since the claims recites "consisting of a contiguous span...". Therefore, it is unclear to the Examiner how a polypeptide consisting of amino acid positions 200 through 300 of SEQ ID NO:4 can be arrived at from a polypeptide consisting of 100 contiguous amino acids of SEQ ID NO:4. Examiner suggests either cancellation of claims 96 or 109.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections, set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 82-123 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kuzuguchi et al. and/or Ping-Fan and Riggs et al.

Claims 82-109 are drawn to polypeptides consisting of a continuous span of 6-100 amino acids of SEQ ID NO:4, wherein the polypeptide has GGPPS activity.

Claims 110-123 are drawn to polypeptides consisting of a continuous span of 6-100 amino acids of SEQ ID NO:4 fused to a heterologous polypeptide sequence, wherein the polypeptide has GGPPS activity.

Kuzuguchi et al. (form PTO-892) discloses a human GGPPS that is 100% identical to SEQ ID NO:4 of the instant invention (see page 5892 and Sequence Alignment). Although fragments consisting of a span of 6-100 contiguous amino acids of hGGPPS are not explicitly disclosed in Kuzuguchi et al., Kuzuguchi et al. discloses

cDNA fragments of hGGPPS gene, fragments of hGGPPS derived from demand degradation and polynucleotides hybridizing to said cDNA fragments (pages 5889-5891). Therefore, the reference of Kuzuguchi et al. anticipates claims 82-109.

Alternatively, it would have been obvious to one having ordinary skill in the art to make enzymatically active fragments of SEQ ID NO:4 and fuse a heterologous polypeptide sequence to said fragment.

Ping-Fan (US Patent No. 5,849,882 – form PTO-892) discloses making enzymatically active fragments of a protein by hydrolysis of the protein, containing about 5-75 amino acids (Column 3 and 5-6).

Riggs et al. (form PTO-892) discloses fusing heterologous polypeptides to a protein of interest to facilitate expression and purification of said protein (16.4.1-16.4.4).

Therefore, combining the teachings of the above references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make fragments of SEQ ID NO:4 having GGPPS activity using the polypeptide taught by Kuzuguchi et al. and using Ping-Fan and also to fuse heterologous polypeptides to said enzymatically active fragments as taught by Riggs et al. One of ordinary skill in the art would have been motivated to make such enzymatically active fragments of GGPPS of Kuzuguchi et al. in order to reduce the size of the enzyme. One of ordinary skill in the art would have been motivated to fuse heterologous polypeptides to said enzymatically fragments of GGPPS of Kuzuguchi et al. in order to effectively purify the polypeptide. One of ordinary skill in the art would have had a reasonable expectation of success in making said fragments and fusion polypeptides consisting of

fragments of the GGPPS of Kuzuguchi et al. since Ping-Fan teaches how to make enzymatically active fragments of a protein of interest. One of ordinary skill in the art would have had a reasonable expectation of success in since the art teaches successful method of trimming enzymes and also making fusion polypeptides of them.

Therefore, Kuzuguchi et all, Ping-Fan and Riggs et al. render claims 82 and 97-123 *prima facie* obvious to those skilled in the art.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Manjunath Rao
Primary Patent Examiner 1652